Strategies for treating and managing testicular cancer

Author: Ruth Dunleavey, BSc, RGN, is clinical research nurse, St Vincent’s Hospital, Sydney, Australia.


Testicular cancer is a malignant neoplasm of the testis that carries an extremely favourable survival rate with current treatment strategies. This article discusses its aetiology, presentation, risk factors and diagnosis. Management strategies fall into two categories depending on subtype. Both are discussed for early and for late stage disease.

Presentation: Testicular cancer usually presents as a painless enlargement in one testis. A normal testis is homogenous in consistency and freely moveable. Any nodular, hard or fixed area in the testis must be considered neoplastic until proven otherwise. There may be abdominal pain with large retroperitoneal metastases. Acute pain is rare unless there is concomitant epididymitis. One in ten men report a history of testicular trauma (Kundra, 2004).

Testicular cancer may be preceded by carcinoma in situ (CIS) which is asymptomatic. About 5% of testis cancer patients will have CIS in their contralateral tests. This progresses to invasive cancer in 50% of cases (Holzbeierlein et al, 2003). If CIS is diagnosed (through biopsy), prophylactic radiotherapy may be implemented (Jones and Vasey, 2003).

Causation and risk factors: Although testicular cancer has a genetic component, incidence of a positive family history is as low as 2%. However, brothers of men with testicular cancer are 6–10 times more likely to develop the disease (Dearnley and Huddart, 2001). All cases share alterations on chromosome 12 and the disease may be caused by a combination of genetic and environmental factors. The age distribution of the disease suggests a prenatal initiating event followed by tumour development from adolescence. Cryptorchidism (undescended testes in childhood) is the only confirmed risk factor.

Histology: Ultrasound is the imaging modality of choice and is generally diagnostic. CT scanning is not used diagnostically but may be used to establish whether there is metastatic disease (Kundra, 2004). A full histological diagnosis is generally not made until an orchidectomy has been performed. Germ cell cancers are almost equally differentiated into seminoma and non-seminoma (Jones and Vasey 2003a) (Table 1). The other main diagnostic feature is elevation of the tumour markers human chorionic gonadotrophin (HCG) and alpha fetoprotein (AFP). Concentrations of AFP are raised in 50–60% of non-seminomatous tumours (but not in pure seminomas). HCG is elevated in 30–35% of non-seminomatous tumours and 10–15% of seminomas (Dearnley and Huddart, 2001).

Lactic dehydrogenase (LDH) is also considered to be an indicator of tumour burden, growth rate and cellular proliferation.
TABLE 1. COMPARISON OF SEMINOMATOUS AND NON-SEMINOMATOUS TUMOURS

<table>
<thead>
<tr>
<th>SEMINOMA</th>
<th>NON-SEMINOMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequently appears in fourth decade of life</td>
<td>Frequently appears in third decade</td>
</tr>
<tr>
<td>High radiosensitivity</td>
<td>Radio-resistant, chemo-sensitive</td>
</tr>
<tr>
<td>15% of patients thought to be stage I pre-operatively will have retroperitoneal metastases</td>
<td>30% of patients thought to be stage I pre-operatively will have retroperitoneal metastases</td>
</tr>
<tr>
<td>AFP (alpha fetoprotein) not raised</td>
<td>AFP raised in 50–60% of tumours</td>
</tr>
<tr>
<td>Cure rate 90% (all stages combined). Early stage disease cure rate 100%</td>
<td>Cure rate &gt;95% stages I and II, 70% stages III and IV</td>
</tr>
</tbody>
</table>

*Source: Jones and Vasey (2003a)*

**Staging**

Staging involves scanning the abdomen and chest to assess for the presence of metastatic disease. CT scanning may be associated with false positives and negatives and therefore some practitioners advocate MRI scanning, certainly in cases where the patient cannot take contrast.

**Management**

The first line of management is surgical. An orchidectomy is performed. A prosthetic testicle may be inserted and also a biopsy of the contralateral testicle may be considered at this stage to detect CIS. If tumour markers have been elevated pre-surgery, they should normally fall in the following days. The half-life of AFP is five days and of HCG is one to two days. The principal prognostic indicator of relapse is vascular invasion of the tumour. Half of primary tumours are associated with vascular invasion (Dearnley and Huddart, 2001). The German Testicular Study Group published data on the complications associated with retroperitoneal lymph node dissection (RPLND) (Heidenreich et al, 2003). Of these complications, 19.7% were minor (superficial wound infection, intestinal paralysis, lymphocele) and 5.4% were major (chyloous ascites, pulmonary embolism, hydronephrosis, small bowel obstruction). A proportion of patients may also experience infertility due to ejaculatory failure, although more modern surgical techniques have substantially reduced this (Rudberg et al, 2002).

**Surveillance**

Surveillance with no further treatment unless the patient relapses is the current standard in the UK. For 70% of patients this is ideal because they will require no further treatment and are effectively cured. Conversely 30% of patients will relapse in a median time of five to six months. Chemotherapy is as efficacious if given in relapse as if it is given adjuvantly post surgery and generally three or four courses will be required.

**Non-seminoma – early stage**

The physician is faced with three options following surgery – surveillance – survival is close to 100% whichever strategy is taken (Dearnley and Huddart, 2001).

**Retroperitoneal lymph node dissection**

Approximately 30% of patients who have stage I disease will have or will go on to develop retroperitoneal nodal involvement, usually within six months of orchidectomy (Scholz and Holtl, 2003). Of these complications, 19.7% were minor (superficial wound infection, intestinal paralysis, lymphocele) and 5.4% were major (chyloous ascites, pulmonary embolism, hydronephrosis, small bowel obstruction). A proportion of patients may also experience infertility due to ejaculatory failure, although more modern surgical techniques have substantially reduced this (Rudberg et al, 2002).

**Surveillance**

Surveillance with no further treatment unless the patient relapses is the current standard in the UK. For 70% of patients this is ideal because they will require no further treatment and are effectively cured. Conversely 30% of patients will relapse in a median time of five to six months. Chemotherapy is as efficacious if given in relapse as if it is given adjuvantly post surgery and generally three or four courses will be required.

**Non-seminoma – early stage**

The physician is faced with three options following surgery – survival is close to 100% whichever strategy is taken (Dearnley and Huddart, 2001).

**Retroperitoneal lymph node dissection**

Approximately 30% of patients who have stage I disease will have or will go on to develop retroperitoneal nodal involvement, usually within six months of orchidectomy (Scholz and Holtl, 2003). Of these complications, 19.7% were minor (superficial wound infection, intestinal paralysis, lymphocele) and 5.4% were major (chyloous ascites, pulmonary embolism, hydronephrosis, small bowel obstruction). A proportion of patients may also experience infertility due to ejaculatory failure, although more modern surgical techniques have substantially reduced this (Rudberg et al, 2002).

**Surveillance**

Surveillance with no further treatment unless the patient relapses is the current standard in the UK. For 70% of patients this is ideal because they will require no further treatment and are effectively cured. Conversely 30% of patients will relapse in a median time of five to six months. Chemotherapy is as efficacious if given in relapse as if it is given adjuvantly post surgery and generally three or four courses will be required.

**Non-seminoma – early stage**

The physician is faced with three options following surgery – survival is close to 100% whichever strategy is taken (Dearnley and Huddart, 2001).

**Retroperitoneal lymph node dissection**

Approximately 30% of patients who have stage I disease will have or will go on to develop retroperitoneal nodal involvement, usually within six months of orchidectomy (Scholz and Holtl, 2003). Of these complications, 19.7% were minor (superficial wound infection, intestinal paralysis, lymphocele) and 5.4% were major (chyloous ascites, pulmonary embolism, hydronephrosis, small bowel obstruction). A proportion of patients may also experience infertility due to ejaculatory failure, although more modern surgical techniques have substantially reduced this (Rudberg et al, 2002).

**Surveillance**

Surveillance with no further treatment unless the patient relapses is the current standard in the UK. For 70% of patients this is ideal because they will require no further treatment and are effectively cured. Conversely 30% of patients will relapse in a median time of five to six months. Chemotherapy is as efficacious if given in relapse as if it is given adjuvantly post surgery and generally three or four courses will be required.

**Non-seminoma – early stage**

The physician is faced with three options following surgery – survival is close to 100% whichever strategy is taken (Dearnley and Huddart, 2001).

**Retroperitoneal lymph node dissection**

Approximately 30% of patients who have stage I disease will have or will go on to develop retroperitoneal nodal involvement, usually within six months of orchidectomy (Scholz and Holtl, 2003). Of these complications, 19.7% were minor (superficial wound infection, intestinal paralysis, lymphocele) and 5.4% were major (chyloous ascites, pulmonary embolism, hydronephrosis, small bowel obstruction). A proportion of patients may also experience infertility due to ejaculatory failure, although more modern surgical techniques have substantially reduced this (Rudberg et al, 2002).

**Surveillance**

Surveillance with no further treatment unless the patient relapses is the current standard in the UK. For 70% of patients this is ideal because they will require no further treatment and are effectively cured. Conversely 30% of patients will relapse in a median time of five to six months. Chemotherapy is as efficacious if given in relapse as if it is given adjuvantly post surgery and generally three or four courses will be required.

**Non-seminoma – early stage**

The physician is faced with three options following surgery – survival is close to 100% whichever strategy is taken (Dearnley and Huddart, 2001).

**Retroperitoneal lymph node dissection**

Approximately 30% of patients who have stage I disease will have or will go on to develop retroperitoneal nodal involvement, usually within six months of orchidectomy (Scholz and Holtl, 2003). Of these complications, 19.7% were minor (superficial wound infection, intestinal paralysis, lymphocele) and 5.4% were major (chyloous ascites, pulmonary embolism, hydronephrosis, small bowel obstruction). A proportion of patients may also experience infertility due to ejaculatory failure, although more modern surgical techniques have substantially reduced this (Rudberg et al, 2002).

**Surveillance**

Surveillance with no further treatment unless the patient relapses is the current standard in the UK. For 70% of patients this is ideal because they will require no further treatment and are effectively cured. Conversely 30% of patients will relapse in a median time of five to six months. Chemotherapy is as efficacious if given in relapse as if it is given adjuvantly post surgery and generally three or four courses will be required.
of tumours with vascular invasion managed by orchidectomy alone will develop recurrent disease (Scholz and Holtl, 2003). Histological type and tumour size may also be of prognostic significance according to some series (Scholz and Holtl, 2003).

**Chemotherapy**

BEP (bleomycin, etoposide, cisplatin) chemotherapy is the regimen of choice for early disease. As an adjuvant treatment after surgery two cycles of chemotherapy are generally adequate. This has not been shown to cause long-term toxicities such as infertility or secondary leukaemias, which are potential complications of heavier treatment regimens used for progressive disease (Scholz and Holtl, 2003).

The advantage of using chemotherapy initially is that it reduces the pressure on intense follow-up following surgery and reassures patients that everything is being done to eradicate the disease.

**Chemotherapy toxicities**

In the short term chemotherapy can cause nausea, vomiting and potentially life-threatening bone marrow suppression, making individuals susceptible to neutropenic sepsis. Cisplatin is nephrotoxic and ototoxic. Because of the high survival rate there is a substantial amount of research looking at long-term toxicities among patients. Toxicities need to be carefully considered when deciding to pursue adjuvant chemotherapy. Most long-term surveys have shown that 10–25% of survivors will have persistent physical symptoms following chemotherapy (Fossa, 2003). Bleomycin is toxic to the lungs, causing fatal pneumonitis in 0.5–1% of patients. Risk factors for this include being older than 40 years, smoking and having a history of pulmonary disease and impaired renal function (Dearley and Huddart, 2001). Cisplatin may damage both peripheral and sensory nerves. It is also known to affect the auditory nerves, causing hearing problems. Long-term ototoxicity, including hearing loss and tinnitus, has been reported in 20–25% of patients (Fossa et al, 2003). Peripheral neuropathies resolve in 6–12 months in most cases.

Chemotherapy often causes azoospermia, which is reversible in 70–80% of cases (Dearley and Huddart, 2001). In one study, 19.5% of patients had confirmed infertility after treatment (Rudberg et al, 2002). Sperm can be banked before chemotherapy or RLTND.

Other long-term toxicities include an increased risk of cardiac events (Huddart et al, 2003) and a higher rate of second malignancies. Some survivors report sexual problems (Joly et al, 2002; Vaughn et al, 2002).

**Seminomas – early stage**

Seminomas have a cure rate of over 90% and with early disease this figure is closer to 100%. Seven in ten men with seminomas have stage I disease. Early stage seminomas are usually treated with adjuvant radiotherapy post-surgery because 15% of stage I or II tumours will have occult retroperitoneal nodal spread that can be cured with radiotherapy. Adjuvant radiotherapy is generally well-tolerated.

The most commonly reported long-term complication is peptic ulcer occurring in 1.6–7.6% of patients (Grossfeld et al, 1998). In addition there is a risk of second malignancies including primaries in the upper gastrointestinal tract and bladder, leukaemia and reduced fertility in the remaining testis (Jones and Vasey, 2003a).

**Advanced disease and relapse**

A small number of men with testicular cancer will present with metastatic disease. Similarly a small number will fail to respond to conventional therapy.

**Pattern of metastasis of testicular cancer**

Testicular cancer tumours can metastasise lymphatically or via the blood. The lymphatic drainage pattern for the testes follows the path of the gonadal veins. Lymphatic metastases from a tumour in the left testicle may be found in the retroperitoneum at the level of the left renal vein. Contralateral involvement is less common but may be found with increased tumour burden. Haematological spread is commonly to liver and lung.

Standard treatment for metastatic disease is chemotherapy using the BEP regimen, with an overall cure rate of 80% for patients with good prognostic features. There is no real consensus on management after failure of BEP. Ifosfamide has been used in salvage regimens as well as high-dose chemotherapy regimens with peripheral blood stem cell rescue. This approach remains experimental (Miki and Nakao, 2002).

For seminomatous tumours in the earlier stages of relapse (stage II), radiotherapy alone may be used. More advanced disease will also require chemotherapy incorporating regimens similar to those described above. Sometimes surgical resection of residual masses will follow or high dose chemotherapy and stem cell rescue may be used (Jones and Vasey, 2003b).